

# Scientists develop nanoparticles to battle cancer

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On a quest to modernize cancer treatment and diagnosis, an MIT professor and her colleagues have created new nanoparticles that mimic blood platelets. The team wants to use these new multifunctional particles to carry out different medical missions inside the body, from imaging to drug delivery.

After years of research, "we still treat cancer with surgery, radiation and chemotherapy," said Sangeeta Bhatia, an associate professor in MIT's Department of Electrical Engineering and Computer Science and the Harvard-MIT Division of Health Sciences and Technology. "People are now starting to think more in terms of 'Fantastic Voyage,' that sci-fi movie where they miniaturized a surgical team and injected it into someone."

The National Cancer Institute has recognized the value of Bhatia's work and has awarded her a grant to continue this line of research. Bhatia and collaborators Michael J. Sailor, chemist and materials scientist at the University of California at San Diego, and Erkki Ruoslahti, tumor biologist at the Burnham Institute for Medical Research, will receive \$4.3 million in funding over five years.

The grant will allow the team to continue work on promising nanoparticle solutions that, while not quite miniature surgical teams, do have the potential to help identify tumors and deliver chemotherapy locally.

One solution already under way involves using nanoparticles for cancer imaging. By slipping through tiny gaps that exist in fast-growing tumor blood vessels and then sticking together, the particles create masses with enough of a magnetic signal to be detectable by a magnetic resonance imaging (MRI) machine. "This might allow for noninvasive imaging of fast-growing cancer 'hot spots' in tumors," said Bhatia. The team will continue this research by testing the imaging capabilities in animal models.

Another solution, described in the Jan. 16 issue of the *Proceedings of the National Academy of Sciences*, is a novel "homing" nanoparticle that mimics blood platelets. Platelets flow freely in the blood and act only when needed, by keying in on injured blood vessels and accumulating there to form clots. Similarly, these new nanoparticles key in on a unique feature of tumor blood vessels.

Ruoslahti had identified that the lining of tumor vessels contains a meshwork of clotted plasma proteins not found in other tissues. He also identified a peptide that binds to this meshwork. By attaching this peptide to nanoparticles, the team created a particle that targets tumors but not other tissues. When injected into the bloodstream of mice with tumors, the peptide sticks to the tumor's clotted mesh.

An unexpected feature of the nanoparticles is that they clump together and, in turn, induce more clumping. This helps to amplify the effects of the particles. "One downside of nanotechnology is that you shrink everything, including the cargo," said Bhatia. "You need particles to accumulate for them to be effective."

The assembly of these new particles concentrates them in a way that may improve on the tumor imaging capabilities the team described earlier. These particles also have the potential to be used as a means to cause clots big enough to choke off the blood supply to the tumor or to deliver

drugs directly into the tumor.

But there are challenges ahead. For one, the team must verify that these particles only accumulate where they are desired. Also, they need better ways to keep the nanoparticles in the bloodstream. The body naturally clears these foreign bodies through the liver and spleen.

The team devised a means to temporarily disable this natural clearing system. They created a "decoy" particle that saturates this clearing system temporarily, allowing the active nanoparticles time to accumulate in the tumor tissue. These decoys, however, were toxic to some mice and also disable a system that normally protects the body, leaving it vulnerable to other invaders.

This challenge dovetails nicely with Bhatia's other work. Not only does she have expertise in liver functions, she directs the facility at the MIT Center for Cancer and Nanotechnology Excellence that analyzes new materials for toxicity and is working to standardize the guidelines for nanomaterial toxicity.

"We need to be able to understand the whole system better to be able to move the field forward," she said.

Source: Massachusetts Institute of Technology

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